Long Term Outcome of PCI vs. CABG in Insulin and Non-Insulin Treated Diabetic Patients Results from the FREEDOM Trial

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Disclosure Statement of Financial Interest

Nothing to disclose

Background

- Global prevalence of adult diabetes mellitus currently exceeds 6.4% (285 mill.), projected to 7.7% (439 mill.) in 2030
- 26 % of the diabetic US population is treated with insulin
- ITDM patients have risk of CV events after PCI, and higher risk of wound infections and mortality after CABG
- FREEDOM trial: Compared to PCI, CABG reduced mortality and MI with a higher rate of stroke in diabetic patients (ITDM and non-ITDM) with MVD

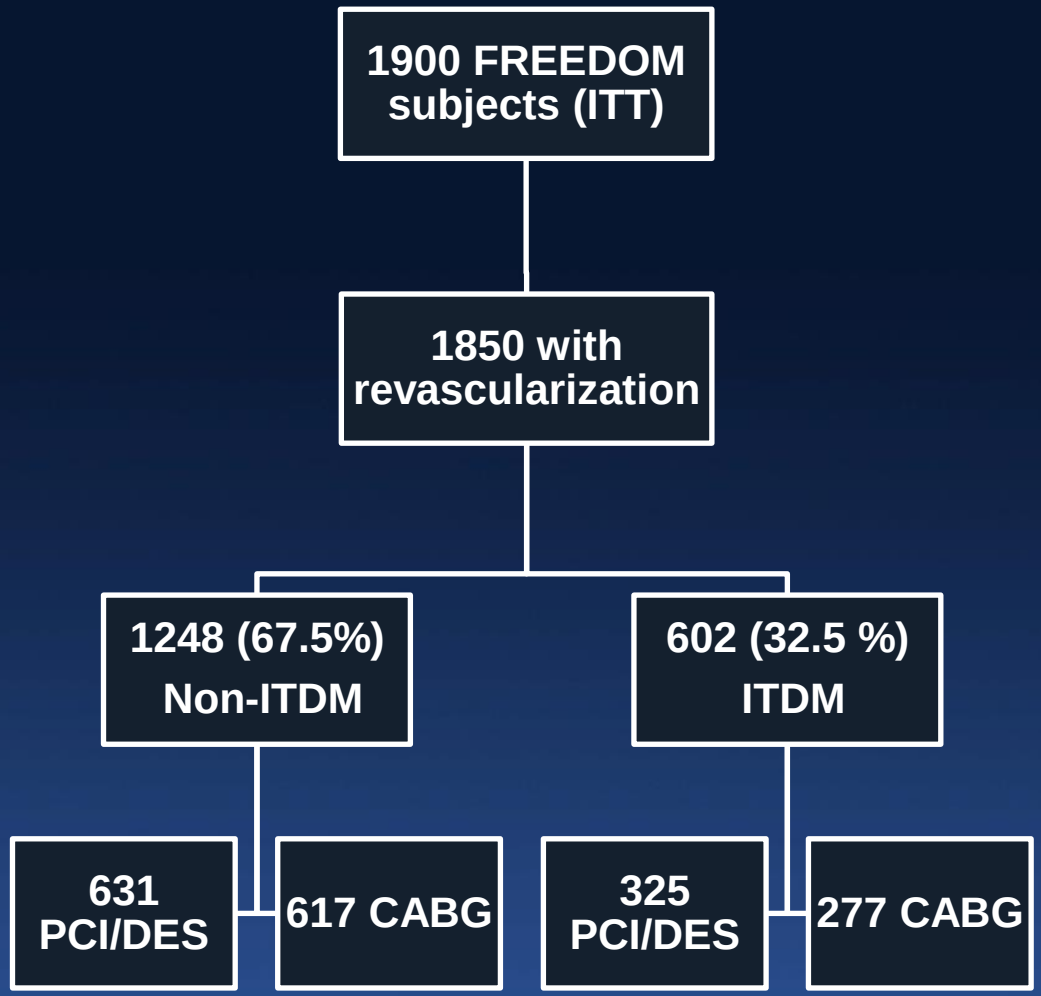
Aims

- To provide a baseline clinical and angiographic description of the ITDM and non-ITDM groups
- To examine whether outcomes by PCI or CABG depend on ITDM
- To examine the influence of ITDM status on the comparison of PCI vs. CABG on the FREEDOM trial primary composite outcome (all-cause death, nonfatal MI, nonfatal stroke)

Study population

Design

- Subgroup analysis of FREEDOM trial
- DM with MVD randomized 1:1 to CABG or PCI/DES
- Stenosis >70% in >2 major vessels. No LM stenoses.
- ≥2 separate territories
- Mostly sirolimus & paclitaxel DES
- ITDM = insulin at baseline (alone or with oral anti-diabetics)



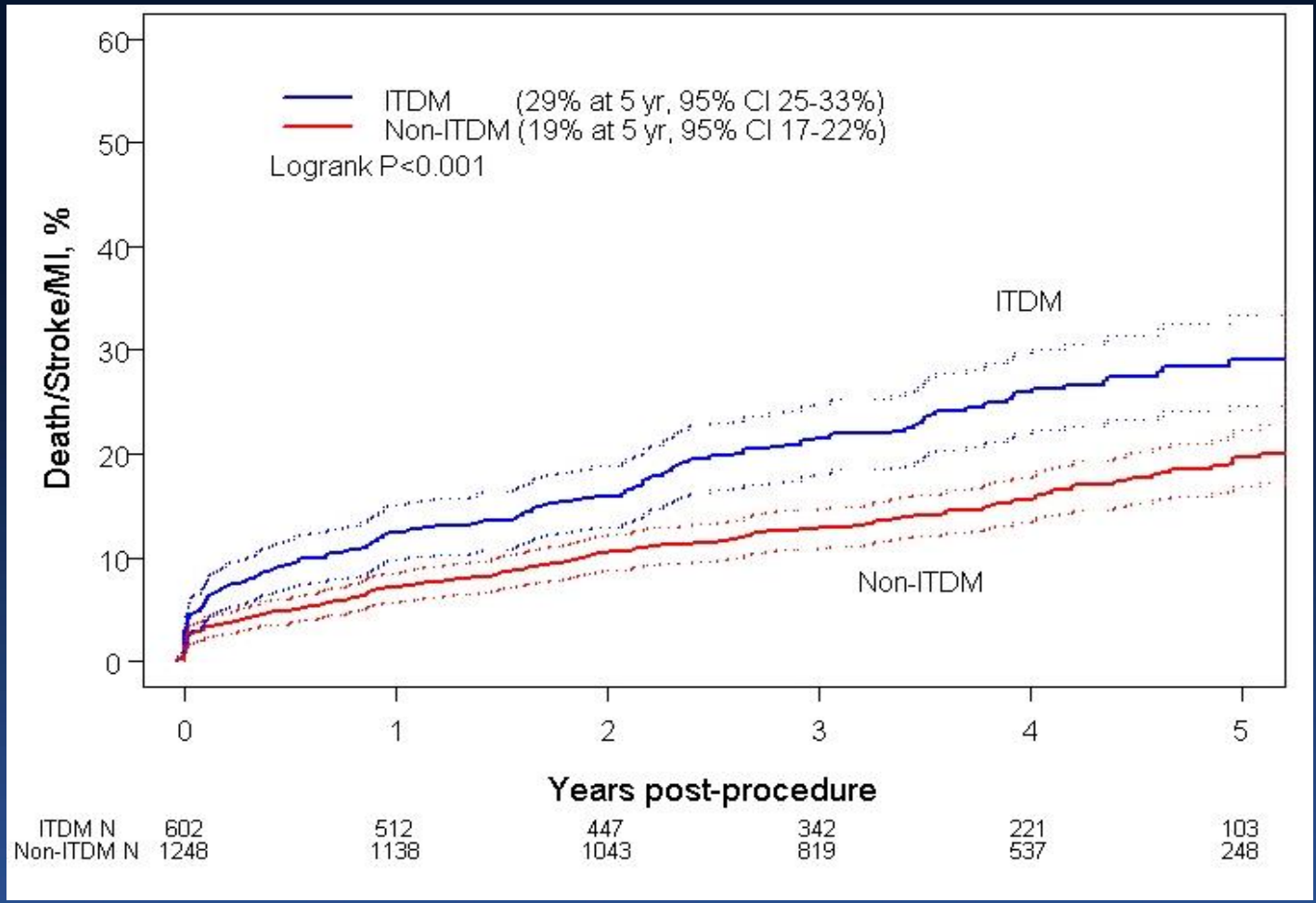
Baseline variables associated with ITDM

	Non-ITDM n = 1248	ITDM n = 602	P Value
Age	63.2 ± 8.9	62.6 ± 9.2	0.16
Male sex	76.5%	61.3%	<.0001
Body mass index (g/m2)	29.3 ± 5.0	30.5 ± 5.9	<.0001
Duration of diabetes (years)	7.7 ± 7.2	15.1 ± 9.9	<.0001
Hemoglobin A1c (%)	7.5 ± 1.6	8.5 ± 1.8	<.0001
Glucose on day of procedure	144.0 (118.8,180.0)	160.0 (126.0,180.0)	<.0001
Blood Urea Nitrogen mg/dL	21.0 (15.4,32.0)	23.1 (16.1,36.0)	0.02
History of hypertension	83.2%	87.5%	0.02
Peripheral neuropathy	5.2%	14.3%	<.0001
Congestive heart failure	24.3%	32.1%	0.0004
NYHA class 1	75.7%	67.9%	0.0004
Acute Coronary Syndrome	28.6%	35.1%	0.005

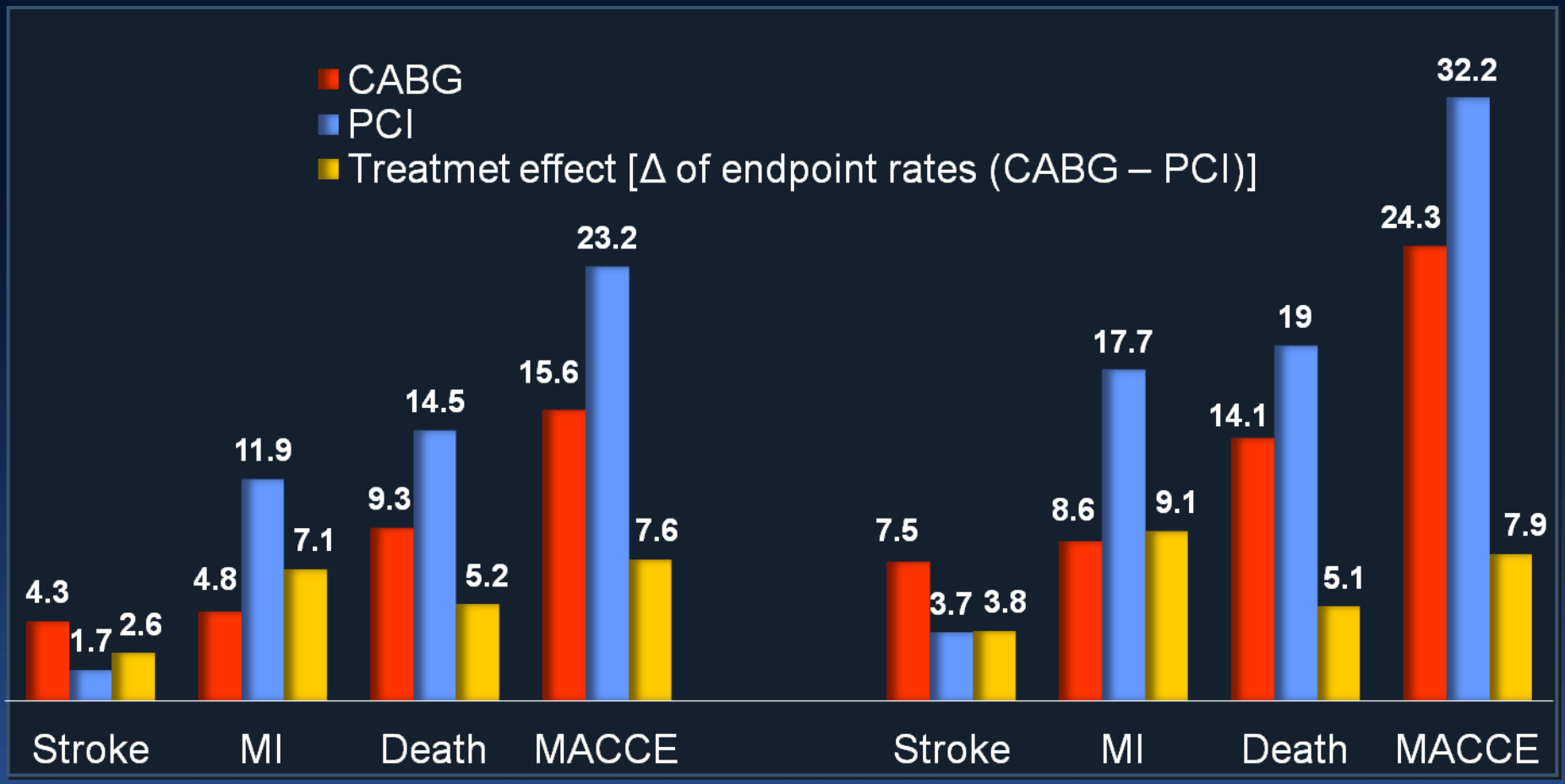
ITDM vs. Non-ITDM Hazard Ratios

	ITDM vs. Non-ITDM HR	95 % CI	P Value
Death/Stroke/MI	1.63	(1.32, 2.02)	<.001
Death	1.54	(1.16, 2.05)	.003
Stroke	1.86	(1.07, 3.02)	.026
MI	1.64	(1.18, 2.30)	.004
CV death	1.58	(1.11, 2.26)	.012
30-Day MACCE	1.54	(1.02, 2.33)	.040
1-Year MACCE	1.51	(1.18, 1.92)	.001
30-Day revascularization	1.20	(0.64, 2.27)	.57
1-Year revascularization	1.44	(1.05, 1.97)	.025
Death/Stroke/MI	1.63	(1.32, 2.02)	<.001
Death	1.54	(1.16, 2.05)	.003
Stroke	1.86	(1.07, 3.02)	.026

Event-Free estimates of the primary composite outcome by insulin use



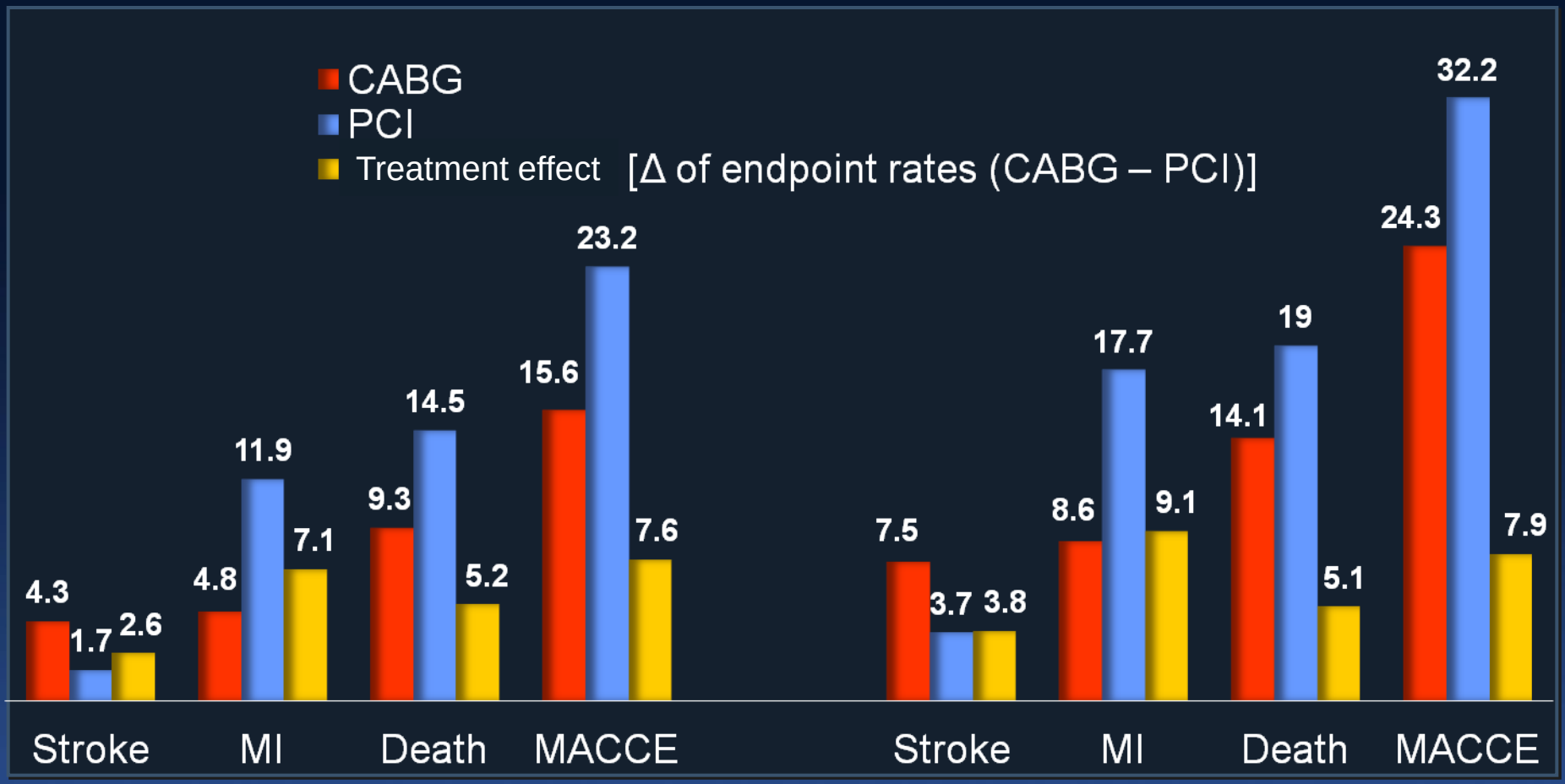
5-Year Kaplan-Meier Event-Free Estimated Event Rates for primary endpoint and



Non-ITDM → ***ITDM***

1.5 Hazard Ratio

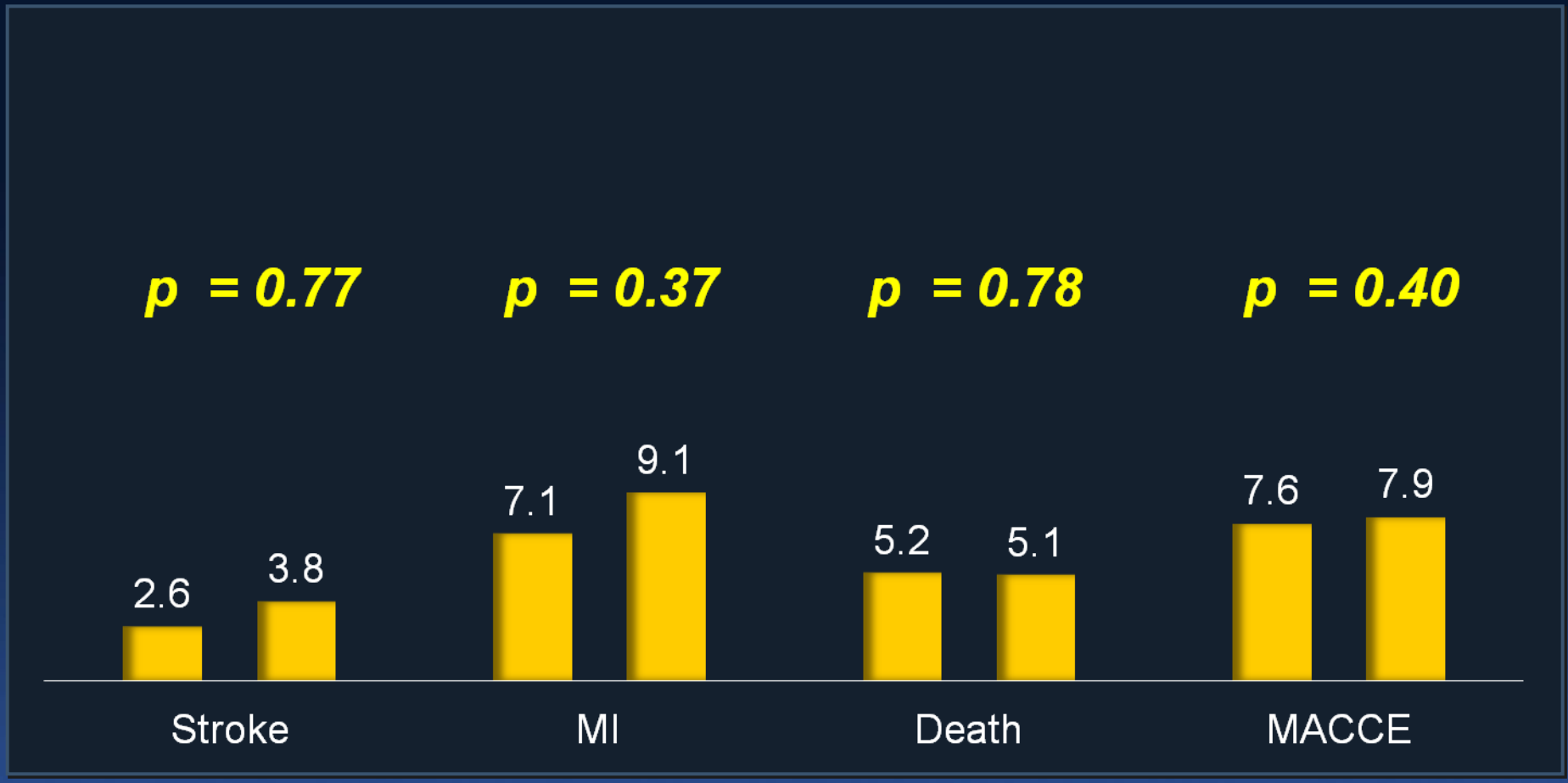
5-Year Kaplan-Meier Event-Free Estimated Event Rates for primary endpoint and



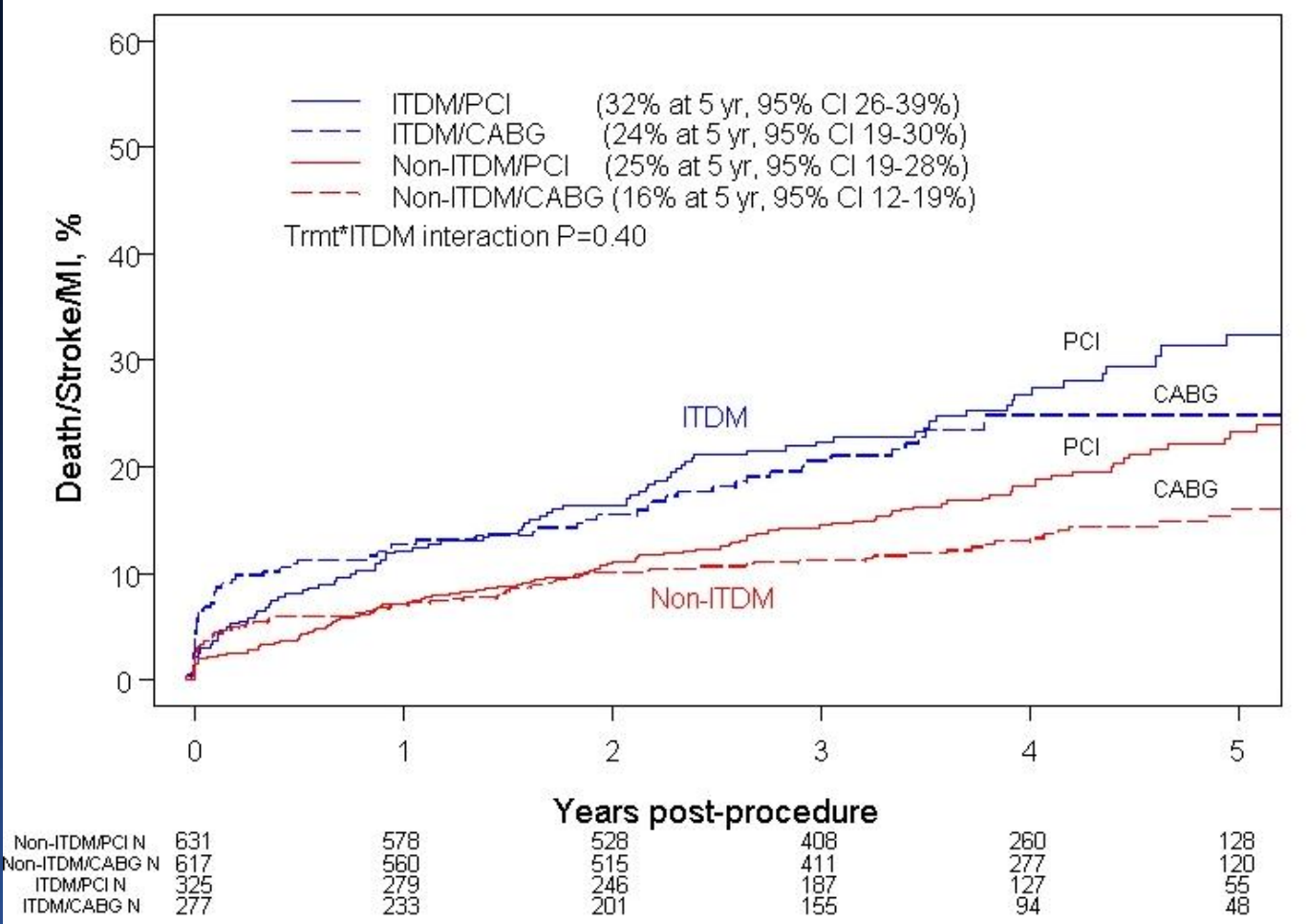
Non-ITDM → ***ITDM***

1.5 Hazard Ratio

Interaction P-value for treatment by insulin dependency status



Event-Free estimates of the primary composite outcome by treatment received and insulin use



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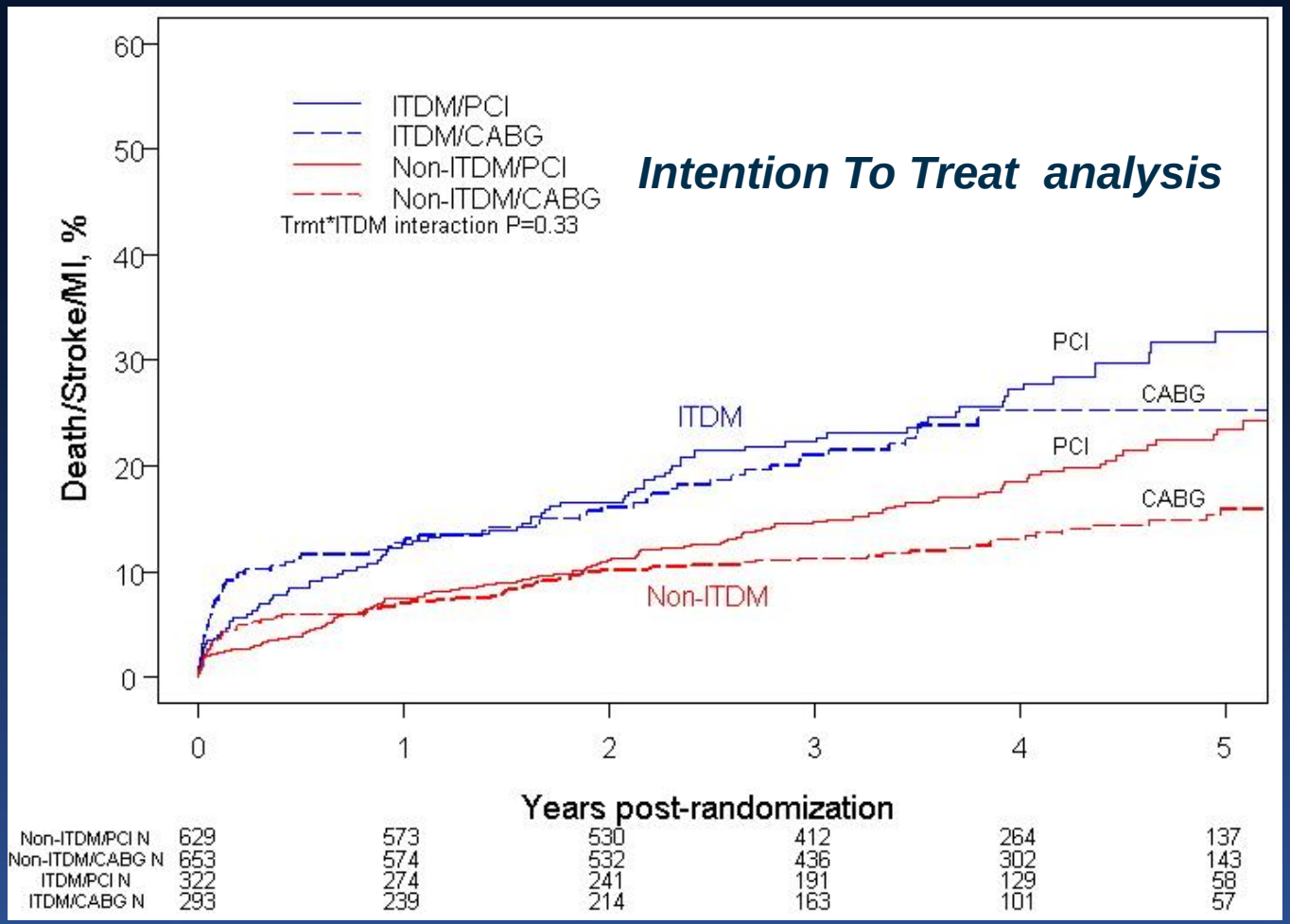
Event-Free estimates of the primary composite outcome by treatment received and insulin use



5-Year Kaplan-Meier Estimated Event Rates, HR for Death/Stroke/MI and interaction P value for treatment by insulin dependency status, at each level of angiographic complexity.

	Non-ITDM			ITDM			Treatment x Insulin
Group	PCI	CABG	HR PCI vs.CABG	PCI	CABG	HR PCI vs.CABG	Interaction P-value
SYNTAX ≤ 22	18.7 (13.0-24.4)	14.1 (9.5-20.75)	1.18 (0.71-1.96)	29.7 (20.2-42.3)	26.3 (17.7-38.0)	1.16 (0.47-1.48)	0.39
SYNTAX 23-32	23.1 (17.8-29.7)	14.3 (10.1-20.0)	1.61 (1.04-2.49)	35.5 (26.8-46.0)	21.8 (15.2-30.7)	1.56 (0.95-2.57)	0.93
SYNTAX ≥ 33	30.4 (20.9-42.8)	20.0 (12.8-30.4)	1.58 (0.88-2.81)	28.9 (19.3-42.0)	25.9 (15.3-41.9)	1.27 (0.61-2.64)	0.65

Limitations

- No randomization with regard to ITDM vs. no ITDM
- Outcome differences between ITDM vs. non-ITDM could be due to
  - residual confounding
  - insulin resistance
  - side effects of insulin treatment

Conclusion

- In patients with diabetes and multi-vessel coronary artery disease there are more major adverse cardiovascular events (death, MI, or stroke) in patients treated with insulin than in those not treated with insulin, but the differences in clinical outcomes between CABG and PCI/DES were maintained regardless of the presence or absence of insulin treatment.